Washington State Department of Health

ELABORATIONS

News and Issues for Washington's Clinical Laboratories

Volume VI Issue 3 April 2001

Measles strikes again! The information you need to know

by Sangeeta Rataul, PhD

Measles is an acute, highly communicable viral disease. Approximately 1 week following exposure, the clinical presentation begins with cough, coryza, conjunctivitis, and fever. This prodromal stage then progresses over the next 3-4 days with all symptoms intensifying and is accompanied by an increasing fever. Fever peaks with the appearance of a rash on the fourth to fifth day. Koplik's spots appear 2-3 days after the onset of the prodrome and shortly before rash onset. These are small, tiny blue-white pinpoint-sized swellings within a reddened area on the buccal mucosa in 50-75% of cases.

Measles infection usually occurs through the inhalation of infected aerosols and droplets produced by infected persons talking, coughing, and sneezing. Measles is highly communicable. Susceptible persons who come in close contact with a measles patient have up to a 99% chance of acquiring the disease.

Persons having the disease are infectious up to one week before and one week after the onset of illness. The most likely settings for exposure to measles infection during the recent resurgence were infectious disease clinics, pediatric emergency rooms, and physician offices.

In the United States, the effective widespread use of measles vaccination has reduced the opportunity for physicians to see clinical features of measles. Atypical presentation in previously immunized persons who failed to seroconvert after one dose of vaccination may present a problem in clinical diagnosis. The use of killed vaccines in the early 1960s placed recipients at risk for "atypical measles" when these individuals were infected by measles virus. These vaccine-failures can show atypical clinical features. The rash begins on hands and feet and spreads towards the trunk, opposite of a normal measles case. As a febrile illness with respiratory symptoms and edema of hands and feet, it can mimic Rocky Mountain spotted fever. No Koplik's spots appear which makes laboratory diagnosis for measles all the more important.

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Meetings to Discuss MTS Fee Change

Several meetings have been scheduled throughout the State to discuss the MTS fee schedule changes. A listing of meeting dates, times, and locations can be found in the chart on page 7.

For a summary of the proposed fee schedule changes, please refer to the March 2001 issue of *Elaborations*.

Measles Update, continued from page 1

Clinical Course of a Typical Case of Measles

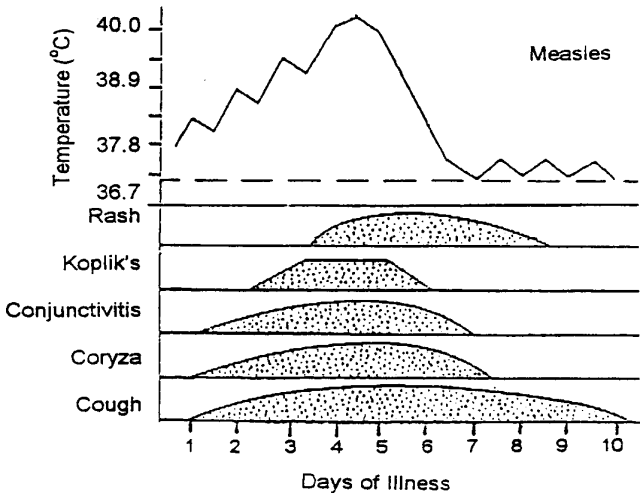

FIG. 1.
Krugman, S.L., Katz, S.L., Gershon, A.A. and Wilfert, C.M. 1985. Infectious Diseases of Children, 8th Ed. St. Louis, MO, C.V. Mosby Company.

Serologic detection is the most versatile and commonly used method for measles diagnosis. Specific IgM antibodies are the first class of serum immunoglobulins to appear following primary measles infection. IgM antibodies can usually be detected within 3 days of rash onset, reach maximum level at about two to three weeks, and then decline to an undetectable level within one to two months. Measles virus IgM antibody can usually be detected in sera in 75 - 80% of individuals by day 2 of rash and detected in 99% of individuals by day 3 of rash.

Current methodology utilized at the Public Health Laboratories (PHL) is the best available, and dramatically reduces the number of false positives. The measles test used by the PHL is a CDC capture EIA for measles virus-specific IgM antibodies using detector monoclonal antibodies (MAbs) to measles virus proteins.

Isolation of Measles virus is performed by inoculating the specimen in mammalian cell culture. If the virus is present in the specimen, it grows and changes the morphology of the cell layer. This is called cytopathic effect or CPE. The cell monolayer is harvested and the virus identified by immunofluorescent staining. Virus isolation is labor intensive and may require several weeks before a culture result can be reported. The sensitivity of virus isolation may be only 25 to 30%. However, isolation of the virus is most important for molecular characterization and is done at Centers for Disease Control and Prevention (CDC). CDC uses this technique to differentiate between wild type and vaccine strains. This information is used to identify the source and to analyze epidemics/clusters. Isolation can be performed from respiratory and urine specimens.

Respiratory Specimens: The preferred specimen is a nasal wash using 3 - 5 ml sterile non-bacteriostatic saline and a bulb aspirator or syringe to rinse the nasal passage. Place all of the recovered wash solution in a tube of viral transport medium (VTM). Another procedure is to use a sterile dacron tipped, wire-stemmed swab to wipe the nasal passage and throat and then place the swab in a tube of viral transport medium. **Collection: Respiratory specimens should be collected during the prodromal phase up to about the first or second day of rash onset but no longer than 4 days after rash onset.**

Urine Specimens: Virus can often be isolated from urine. Collect 50 - 100 ml of clean voided urine in a sterile container. **Collection: Urine specimens may be collected no later than one week after rash onset.**

The type of specimen, collection time relative to onset, and specimen handling are critical in the accurate

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NOTE: Letters to the editor may be published unless specified otherwise by the author.

Website addresses:
DOH home page: http://www.doh.wa.gov
LQA home page:
http://www.doh.wa.gov/hsqa/fsl/LQA_Home.htm

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laboratory diagnosis of measles. To optimize diagnosis, specimens for virus isolation should be collected at the same time the serum specimen is obtained.

Specimen Identification: Each specimen must be *CLEARLY* identified and labeled with patient name or identification number and must be accompanied by a Washington State Public Health Laboratories (PHL) Virus and Rickettsial form. It is extremely important the following information is submitted:

Patient	**Specimen**	**Submitter**
Patient's Name/ID #	Specimen Type	Submitter Name
Date of Birth/Sex	Rash Onset	Address/Phone
Immunization & Travel History	Date of Collection	Contact Person

Packaging and Shipping: Refrigerate all specimens and ship on ice packs. Specimens should be received in the PHL within **24 hours of collection**. Please contact the PHL Virus Unit (206) 361-2874 prior to shipment. Express Mail, UPS, and Federal Express all offer next day delivery. Packages may also be shipped via Greyhound. Greyhound packages are picked up Monday through Saturday at 7:00 a.m.

NOTE: *The PHL Office of Operations and Technical Support provides, at no charge, Virus and Rickettsial Forms, viral transport media (VTM), cardboard cans, biohazard bags, and shipping containers that meet shipping regulations for diagnostic specimens. To order, mail or fax (206) 361-4997 the Requisition Supplies Form or call the Mail Services at (206) 361-2865.*

Results And Interpretation: Collection time of specimens relative to onset date is very important in the interpretation of the results. All laboratory results should be interpreted in conjunction with the clinical findings.

Turn-around Times

Serology:

IgM and IgG Results ..... 24 - 48 hours

Isolation:

Preliminary Result ..... One week
Negative Result ..... 2-4 weeks

Telephone Contacts

Serology Unit ..... (206) 361-2873
Virology Unit ..... (206) 361-2874
Mail Services ..... (206) 361-2865

Epidemiology Immunization – Patricia Dehart ..... (360) 236-3537
Epidemiology Emergency Response ..... (206) 361-2914
(After hours, weekends, and holidays)

Waived Testing Under Review

by Susan Walker

Laboratories possessing a waived license are subject to the least amount of oversight under the federal Clinical Laboratory Improvement Amendments (CLIA) and the state Medical Test Site (MTS) Law. Laboratories are required to possess a current waived license and to follow all manufacturers' instructions as written in a current package insert. Nationally more than 70% of licensed laboratories possess a waived or PPMP license.

A waiver pilot project recently performed in Colorado and Ohio by CLIA surveyors found problems in over 50% of waived and PPMP laboratories. The surveyors found that laboratories did not possess a current set of manufacturers' instructions for the waived tests, or the instructions the laboratories had were from another test system or kit. Some laboratories were not performing required quality control (QC) and others were performing tests outside the scope of their waived or PPMP license.

The Health Care Financing Administration (HCFA) expanded this project to all ten regions of the country and found similar problems in all regions. In the Northwest region, Idaho was the state chosen for inspections of some of its waived and PPMP laboratories.

Under the current MTS and CLIA regulations, waived laboratories need to possess a current set of manufacturers' instructions for all waived test systems used in their facility. It is very important that the instructions are current since the instructions and QC requirements change periodically. For example, the Abbott Signify Strep A kit, which is a waived test system under CLIA, made a modification to its instructions changing its QC instructions from recommended to REQUIRED as of February 2000. According to the package insert all Abbott Signify users MUST run a positive and negative external control with each new lot number of kit and each change in operator (see QC requirements on page 5).

If your laboratory possesses a waived or PPMP license, you may not use any test kit that is not listed as being waived. If you wish to use a non-waived test kit, you must upgrade your MTS license category by contacting the Office of Laboratory Quality Assurance. If you are using your waived test or kit for some use other than what the test or kit was waived for, it becomes a high complexity test. Examples include: running the test using serum when the kit is waived for whole blood only; using a waived rapid Strep A kit to identify colonies isloated from a throat on a blood agar plate; making changes to the reagents or method as written by the manufacturer. Any of these types of changes would change the test to high complexity and the laboratory must meet all requirements for a high complexity test such as proficiency testing, personnel requirements, validation, etc.

Unless the manufacturer's instructions give the laboratory the option of running the test as a waived or moderately complex test, as Roche did for the CoaguChek or CoaguChek S instruments (see article on page 6), the laboratory MUST follow ALL manufacturer's requirements as listed in the waived test package insert. When manufacturer's instructions use the word MUST, the laboratory is required to perform quality control as defined in the package insert. Some instructions state that quality control SHOULD be performed rather than MUST be performed. While these instructions are not mandatory, good laboratory practice would be to follow the manufacturer's recommendations for performing quality control to ensure the test is performing properly. Page 5 has a representative sample of some waived test systems that have specific QC requirements that MUST be performed. Please review your current package inserts to make sure that you are following the manufacturer's instructions correctly.

NOTE: If you are accredited by an outside accrediting agency (CAP, JCAHO, COLA, AABB, AOA, ASHI), please refer to their standards regarding waived testing since they may differ from the information presented here.

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Examples of Waived Test Systems With Specific Quality Control Requirements

Analyte	Test system	Quality control requirements
Helicobacter pylori antibody	Quidel QuickVue One-Step H. pylori WB	A positive and negative control must be tested when opening a new test kit. Each operator performing testing within a test kit must test a positive and negative control once with each test kit.
Strep antigen	Abbott Signify Strep A	Positive and negative external controls must be tested when opening a new test kit and each operator performing testing within a test kit must test a positive and negative external control once with each 25 test kit
Strep antigen	Quidel QuickVue In-Line One-Step Strep A	A positive and negative external control must be tested when opening a new test kit. Each operator performing testing within a kit must test a positive and negative external control once with each 25 test kit.
Strep antigen	Wyntek OSOM Strep A Test	Positive and negative external controls must be tested when opening a new test kit and each operator performing testing within a test kit must test a positive and negative external control once with each 25 test kit
Urinalysis	Roche/Boehringer Mannheim Chemstrip 101 Urine Analyzer	Positive and negative controls must be tested daily, when a new vial of strips is opened (including every lot change), and when calibration is performed

Comments Requested By FDA

The Food & Drug Administration (FDA) is soliciting comments on its recently published "Guidance for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Criteria for Waiver". A notice announcing the guidance document was published in the March 1, 2001 Federal Register and can be reviewed at www.fda.gov/cdrh/ode/guidance/1147.pdf.

Responsibility for determining whether a particular device is waived under CLIA was transferred from the Centers for Disease Control and Prevention (CDC) to FDA on January 21, 2000. Prior to this transfer, proposed criteria used by CDC for waiver classification were published in the Federal Register on September 13, 1995. The CDC and HCFA criteria required demonstration of accuracy by comparison of test results to the value of reference materials. These proposed rules were never finalized.

In the recently published Federal Register notice, FDA states that, based on its interpretation of the legislative history and the changes to the CLIA statute enacted by Congress on November 21, 1997 (part of the FDA Modernization Act of 1997), alternative criteria to the criteria proposed by HCFA and CDC can be used to determine whether a device can be waived. The most significant difference between the criteria proposed by CDC and HCFA and the criteria proposed by FDA is in demonstration of accuracy of the device. The FDA draft guidance allows accuracy to be demonstrated solely by studies that compare the performance of the device in the hands of untrained users with the performance of the device in the hands of individuals that meet the qualifications to perform moderate or high complexity testing under CLIA.

If you are interested in providing comments on the proposed FDA criteria, please submit written comments on the draft guidance by May 30, 2001 to the Dockets Management Branch (HFA-305), Food & Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Comments should be identified with the docket number, 01D-0044.

NOTE: The most current list of waived tests can be found at www.doh.wa.gov/hsqa/fsl/LQA_Home.htm.

Attention All CoaguChek And CoaguChek S Users

The CoaguChek manufactured by Roche Diagnostics is a point of care instrument for the measurement of prothrombin time from a drop of capillary or venous whole blood. The protime is performed automatically as soon as the sample is applied. The result is given in seconds as well as an INR.

In a letter dated April 2, 1999, Roche gave their CoaguChek users the option of running the CoaguChek as a moderately complex instrument even though it had been granted waived status under CLIA . Roche explained in their letter that if a laboratory chooses to run the CoaguChek as a moderate complexity test, they must follow all CLIA requirements including training documentation, quality control (QC) documentation, and proficiency testing. Roche also stated that the laboratory must meet all licensing requirements for a moderate complexity laboratory which means that the laboratory must possess a license higher than waived or PPMP and be subject to inspection.

Since the CoaguChek manufacturer instructions offer this dual complexity level QC program, the Office of Laboratory Quality Assurance (LQA) will recognize both of these methods as options for the CoaguChek system as long as you have a package insert that provides for this option. (See QC requirements below). If you are a moderate complexity laboratory and choose the moderate complexity method of QC requirements, you MUST notify LQA of your decision to run protimes as a regulated test that makes it subject to inspection. If you currently possess a Waiver or PPMP license and are running the QC requirements for a moderately complex laboratory, you must send LQA a letter requesting a category upgrade to your license. If you choose not to upgrade your license, you are required to follow the QC instructions for a waived instrument that includes weekly liquid controls performed by each operator (see requirements below).

Your laboratory MUST also be enrolled in a five sample approved proficiency testing (PT) program if you choose to run the moderately complex requirements. Your PT results must be mailed or faxed to our office since most PT companies list protime by CoaguChek as a waived test and LQA may or may not electronically receive your results.

Information from *CoaguChek Electronic QC Users Manual*

"**Frequency of Testing Requirements - Waived Testing:**

Daily Requirements:
Two levels of Electronic Quality Control (Cat. No. 2032155) or two levels of liquid controls must be tested to verify proper monitor performance.

Weekly Requirements:
Each operator performing CoaguChek or CoaguChek S testing must test two levels of liquid quality control and achieve results within the designated range.

Additional requirements:

1. Two levels of liquid control must be tested and results must be within the designated range for the following situations:
   - You open a new test kit
   - You suspect improper storage or handling of the strips
   - Patient PT results are unusually high or low
2. Two levels of Electronic Quality or two levels of liquid quality control must be tested if the monitor is dropped or mishandled. The results must be within the designated ranges."

"Frequency of Testing Requirements - Moderate Complexity Testing:

Daily quality control testing is good laboratory practice. It is also required by most states and by CLIA '88 regulations. Check with the appropriate licensing or accrediting bodies to ensure that your quality control program meets established standards.

Daily Requirements:
A two level Electronic Quality Control cartridge (Cat. No. 2032155) or Liquid Quality Controls may be tested to verify proper monitor performance.

Additional requirements:
A Liquid Quality Control (Level 1 or 2) should be tested when:

- A new shipment of test strips is received
- A new lot number of strips is opened
- Improper storage or handling of the strips is suspected
- Patient PT results are unusually high or low

This testing is in addition to the daily EQC testing. The results must be within the designated ranges."

MTS Fee Discussion Meeting Schedule

Date / Time	City	Meeting Location
April 19 5:00 - 6:00 pm	Spokane	Doubletree Hotel, Spokane Valley 1100 North Sullivan Road Spokane
April 26 12:30 - 1:30 pm	Shoreline	Public Health Laboratories Room Q-20 1610 NE 150th Street Shoreline
May 1 12:30 - 1:30 pm	Wenatchee	Wenatchee Valley Clinic Conference Room A 820 N Chelan Ave Wenatchee
May 2 12:30 - 1:30 pm	Kennewick	Benton PUD Auditorium 2721 W 10th Avenue Kennewick
May 3 12:30 - 1:30 pm	Yakima	Providence Yakima Medical Center Board Room A/B 110 S. 9th Ave Yakima
May 9 12:00 - 1:00 pm	Tacoma	Jackson Hall Auditorium (the brick building directly across from the main enterance to Tacoma General Hospita) 314 South ML King Jr. Way Tacoma
May 15 12:00 - 1:00 pm	Mount Vernon	Affiliated Health Services Skagit Campus San Juan Room 1415 E. Kincaid Street Mount Vernon
May 17 12:00 - 1:00 pm	Olympia	DOH Target Plaza Training Room 2725 Harrison Ave NW, Suite 500 Olympia
May 23 12:00 - 1:00 pm	Vancouver	Southwest Washington Hospital Campus Auditorium A - Educational Building 400 NE Mother Joseph Place Vancouver

NOTE: Since the meetings will be held during the lunch hour, feel free to bring a brown bag lunch.

Meetings to Discuss MTS Fee Change

Several meetings have been scheduled throughout the State to discuss the MTS fee schedule changes. A listing of meeting dates, times, and locations can be found in the chart on page 7.

Since the meetings will be held during the lunch hour, feel free to bring a brown bag lunch.

For a summary of the proposed fee schedule changes, please refer to the March 2001 issue of *Elaborations*.

Calendar of Events

PHL Training Classes:

Lab Regulations: Making Compliance Easier

May 9	Shoreline
May 10	Spokane

Clinically Relevant Microbiology

June 8	Shoreline
June 9	Shoreline

WSSCLS/NWSSAMT Spring Meeting

April 19-21	Spokane

Northwest Medical Laboratory Symposium

October 10 - 13	Portland

8th Annual Clinical Laboratory Conference

November 12	Seattle

Contact information for the events listed above can be found on page 2. The Calendar of Events is a list of upcoming conferences, deadlines, and other dates of interest to the clinical laboratory community. If you have events that you would like to have included, please mail them to ELABORATIONS at the address on page 2. Information must be received at least one month before the scheduled event. The editor reserves the right to make final decisions on inclusion.

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